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Summary and conclusions

Earlier studies, mostly designed to establish the value of various pharmacologic interventions after myocardial infarction, have shown the prognostic value of global left ventricular function, measured as left ventricular ejection fraction (LVEF), in terms of mortality and re-admission rates for heart failure.(1-3) In **chapter 2** we showed that LVEF assessed shortly after primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI), is a powerful predictor of long term survival. However, the post-procedural ECG is available even sooner. In **chapter 3** it was shown that an increasing number of Q-waves on the first 12-lead ECG after PPCI is strongly associated with the extent of myocardial damage, measured as area under the curve of creatin kinase and its myocardial isoenzyme, and adverse long-term prognosis. This easy and low-cost method of clinical assessment after PPCI could lead to more focused use of advanced and expensive additional diagnostics or therapeutics.

In **chapter 4** the relationship between ST-segment resolution, residual ST-segment elevation and Q waves in relation to left ventricular function, size and extent of infarction, and microvascular injury in acute myocardial infarction measured by MRI was explored.

In **chapter 5** we compared electromechanical endocardial mapping (EEM) with MRI and we found that EEM-derived global left ventricular functional parameters showed a significant underestimation compared to MRI. However, regional parameters appeared to be useful indicators of dysfunctional myocardial segments. Although there were substantial differences in global left ventricular functional parameters between EEM and MRI, a good correlation was found between the surface-area of the EEM-map with a unipolar voltage below 6,9 mV and MRI infarct-size.(4) Segmental analyses showed that EEM can be used to determine both regional function and extent of infarction in patients with a large myocardial infarction. Although regional data showed good correlation with MRI, convincing cut-off values for EEM-parameters could not be established. Exact pinpointing of myocardial areas benefiting from direct injection of therapeutics remains difficult.

Since residual left ventricular function was shown to be one of the most powerful predictors of prognosis after primary PCI for STEMI, every effort should be made to conserve, and possibly even improve, left ventricular function after STEMI. Cell therapy has been a promising new modality in the field of post-STEMI care, which has rendered mixed results so far.(5-10) **(chapter 6)** In order to assess the full potential of cell therapy in a national

multicenter trial, a pilot-study was conducted to establish the safety and feasibility of all study related procedures (**chapter 7**). This study indicated that intracoronary infusion of autologous bone marrow derived mononuclear cells after recent myocardial infarction is safe in a multicenter setting. At 4 months follow-up a modest but significant increase in global and regional LV function was observed, with a concomitant decrease in infarct-size.

After successfully completing the pilot-study, the multicenter HEBE trial could be initiated (**chapter 8 and 9)**. The rationale behind the three arm-armed study design is to test the hypothesis that the beneficial effects of cell-therapy on left ventricular function cannot be completely attributed to the formation of new cardiac myocytes or endothelial cells, but that these positive effects could also be a combined effect of all mononuclear cells, through the release of growth factors and cytokines. Intracoronary infusion was chosen as mode of delivery, since the benefits of avoiding local injection were considered to outweigh the obvious drawback of decreased local cell-retention.(11) The rationale behind the choice for MRI as imaging modality for the primary end-point of the study is its ability to combine left ventricular function analysis with infarct-size analyses.

The HEBE trial showed no benefit of infusion of autologous bone marrow derived progenitor cells after STEMI. Research in this field will most likely continue, since cell therapy remains a very appealing concept. In the future trials with other cell types or pre-treatment of cells may be conducted. However, since the procedures involved in cell therapy are relatively invasive and time-consuming, great care should be taken to identify those patients in which the potential of success is the highest and clearly outweighs the procedural risk, costs and patient discomfort.

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